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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,916	07/09/2007	Naoya Kojima	P30703	2020

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EXAMINER	
POPA, ILEANA	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
10/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/598,916	KOJIMA ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8 and 9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/27/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office action.

2. Claims 4-7 have been cancelled. Claim 1 has been amended. Claim 9 is new. Claims 1-3, 8, and 9 are pending and under examination.

3. All rejections pertaining to claims 4-7 are moot because Applicant cancelled the claims in the reply filed on 06/27/2008.

Information Disclosure Statement

4. The IDS form of 06/27/2008 has been considered. It is noted that the Mizuochi reference has been lined through because Applicant did not provide an English translation of the document, nor did Applicant provide an English abstract. Therefore, this document was not considered by the Examiner.

Response to Arguments

Priority

5. With respect to providing a translation of the foreign priority document Applicant states that 37 C.F.R. § 1.55 (a)(4) indicates that the Office is only permitted to comment on a translation of the priority document when the cited art has a date alter than Applicant's priority. Such a statement is incorrect. 37 C.F.R. § 1.55 (a)(4) clearly

indicates that the translation of the foreign priority document is required if specifically requested by the Examiner. Therefore, the Examiner is permitted to comment on a translation. However, the Examiner agrees that, since the cited prior art has a date which is earlier than Applicant's priority date, Applicant does not have to submit an English translation of his priority document at this time.

Claim Rejections - 35 USC § 102

6. The rejection of claims 1-3 are under 35 U.S.C. 102(b) as being anticipated by Sugimoto et al. (U.S. Patent No. 5,759,572) is withdrawn in response to Applicant's amendment to the claims filed on 06/27/2008. Specifically, Applicant amended claim 1 to recite an anti-cancer drug; Sugimoto et al. teach an anti-cancer vaccine and not an anti-cancer drug (it is noted that the instant specification defines anti-cancer drugs as distinct from anti-cancer vaccines, see p. 11, last two paragraphs).

7. Claims 1-3 are under 35 U.S.C. 102(b) as being anticipated by Shimizu et al. (Bioorganic and Medicinal Chemistry, 2003, 11: 1191-1195), as evidenced by Wang et al. (Chin Med J, 2000, 113: 281-285) is withdrawn in response to Applicant's amendment to the claims filed on 06/27/2008. Specifically, Applicant amended claim 1 to recite an anti-cancer drug. Shimizu et al. teach *Leishmania* peptide antigens and not an anti-cancer drug.

Claim Rejections - 35 USC § 103

8. The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Sugimoto et al., in view of each Wang et al., Koenen et al. (Cancer Immunol Immunother, 1996, 42: 310-316), Hagiwara et al. (Cancer Research, 1993, 53: 687-692), and Babincova et al. (Bioelectrochemistry, 2002, 55: 17-19) is withdrawn in response to Applicant's amendment to the claims filed on 06/27/2008. Specifically, Applicant amended claim 1 to recite an anti-cancer drug; the cited references teach an anti-cancer vaccine and not an anti-cancer drug (it is noted that the instant specification defines anti-cancer drugs as distinct from anti-cancer vaccines, see p. 11, last two paragraphs).

New Rejections

Claim Rejections - 35 USC § 112, 2nd paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-3 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claims are indefinite because they recite both a composition and method steps and it is not clear whether the claim is drawn to a composition or to a method of treatment or preventing ischemia in a mammal (see MPEP 2173.05(p) [R-5] II).

For examination purposes, the claims are interpreted as being drawn to a drug delivery composition comprising drug-loaded liposomes (claims 1-3) further comprising liposomes encapsulating a magnetic compound.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-3 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kole et al. (J. Infect. Dis., 1999, 180: 811-820), in view of both Sugimoto et al. (U.S. Patent No. 5,759,572, of record) and Babincova et al. (Bioelectrochemistry, 2002, 55: 17-19, of record).

Kole et al. teach a composition comprising mannosylated liposomes and doxorubicin (i.e., an anti-cancer drug), wherein the composition is useful to deliver doxorubicin to macrophages (claim 1) (Abstract, p. 811, columns 1 and 2, p. 812, column 1).

Kole et al. teach mannosylation by using mannopyranoside and not mannopentaose or mannotriose (claims 1-3). Sugimoto et al. teach mannosylated liposomes comprising liposomes, wherein the liposomes are coated with an oligosaccharide such as manopentaose or mannotriose and wherein the mannosylated

liposomes are capable of delivering therapeutic agents to macrophages (Abstract, column 1, lines 5-10, column 2, lines 24-65, column 7, lines 55-65). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the composition of Kole et al. by replacing their mannopyranoside with manopentaose or mannotriose to achieve the predictable result of obtaining liposomes suitable to delver drugs to macrophages.

Kole et al. and Sugimoto et al. do not teach their composition as further comprising mannosylated liposomes encapsulating a magnetic compound (claim 8). Babincova et al. teach the use of liposomes encapsulating a magnetic compound and doxorubicin for site-specific delivery of doxorubicin, wherein the exposure of liposomes to a magnetic field leads to local hyperthermia followed by the release of doxorubicin from the liposomes (Abstract, p. 117, column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the composition of Kole et al. and Sugimoto et al. by further adding mannosylated liposomes encapsulating a magnetic compound, with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to obtain a composition capable of conditional release of doxorubicin. One of skill in the art would have been expected to have a reasonable expectation of success in doing such because the art teaches that liposomes encapsulating magnetic compounds can be successfully made.

With respect to the limitations of the composition being administered intraperitoneally and delivered to the omentum, it is noted that the claims are drawn to a composition and not to a method of *in vivo* administration; the recitation of

administration *in vivo* is only an intended use which does not state any distinct definition of any of the claimed limitations such as to differentiate the claimed composition from the composition taught by the Kole et al., Sugimoto et al., and Babincova et al.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Applicant's arguments are answered below to the extent that they pertain to the instant rejection.

Applicant argues that in the present invention the liposome composition is taken up by intraperitoneal macrophages within a short period (between thirty minutes and one hour), and 60% of the composition is accumulated in breast tissue within a few hours to twelve hours. This faster delivery and high efficiency is an unexpected result, which is achieved by the drug delivery composition as claimed. Applicant submits that such unexpected results are not suggested by the cited art and could not have been predicted by the art.

Applicant's arguments are acknowledged, however they are not found persuasive because they pertain to a method of *in vivo* drug delivery. As noted above, the claims are drawn to a composition and not to a method of *in vivo* administration; therefore, the argument that the prior art does not suggest fast delivery is irrelevant.

13. Claims 1-3, 8, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimizu et al. (Bioorganic and Medicinal Chemistry, 2003, 11: 1191-1195, of record), in view of each Wang et al. (Chin Med J, 2000, 113: 281-285, of record), Hagiwara et al. (Cancer Research, 1993, 53: 687-692, of record), Kole et al., and Babincova et al.

Shimizu et al. teach a (i) composition comprising oligomannose-coated liposomes and *Leishmania* peptide antigens, wherein the oligomannose is manopentaose (claims 1-3), and (ii) a method of treating *Leishmania* infestation comprising intraperitoneal administration of the composition above (claim 9) (Abstract, p. 11191, column 2, p. 1192, columns 1 and 2). With respect to the limitation of the composition being taken by the macrophages in the peritoneal cavity (claims 1 and 9), Shimizu et al. teach their oligomannose-coated liposomes as being able to efficiently interact with the mannose receptor on antigen-presenting cells (APCs) followed by the delivery of the antigen to the APCs (p. 1194, column 1); since macrophages are APCs (see Wang et al., Discussion), Shimizu et al. teach that their composition is taken up by macrophages in the peritoneal cavity. Since macrophages represent the major constituent of milky spots in the omentum and mesentery (see Hagiwara et al., Abstract, p. 687, column 1, first paragraph and column 2, fifth paragraph, p. 692, column 1, last paragraph), the mannosylated liposomes of Shimizu et al. and Wang et al. must necessarily be targeted to the omentum and mesentery (claims 1 and 9).

Shimizu et al., Wang et al., and Hagiwara et al. teach treating *Leishmania* infestation by using *Leishmania* peptide antigens and not an anti-cancer drug.

However, at the time the invention was made, the use of anti-cancer drugs to treat *Leishmania* infestation was taught by the prior art. For example, Kole et al. teach treating *Leishmania* infestation by using mannosylated liposomes loaded with doxorubicin (Abstract, p. 811, columns 1 and 2, p. 812, column 1). Based on these teachings in the art, it would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Shimizu et al. by replacing their peptide antigens with the doxorubicin of Kole et al. to achieve the predictable result of treating *Leishmania* infestation.

Shimizu et al., Wang et al., Hagiwara et al., and Kole et al. do not teach their composition as further comprising mannosylated liposomes encapsulating a magnetic compound (claim 8). Babincova et al. teach the use of liposomes encapsulating a magnetic compound and doxorubicin for site-specific delivery of doxorubicin, wherein the exposure of liposomes to a magnetic field leads to local hyperthermia followed by the release of doxorubicin from the liposomes (Abstract, p. 117, column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the composition of Shimizu et al., Wang et al., Hagiwara et al., and Kole et al. by further adding mannosylated liposomes encapsulating a magnetic compound, with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to obtain a composition capable of conditional release of doxorubicin. One of skill in the art would have been expected to have a reasonable expectation of success in doing such because the art teaches that liposomes encapsulating magnetic compounds can be successfully made.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Applicant's arguments are answered below to the extent that they pertain to the instant rejection.

Applicant argues that in the present invention the liposome composition is taken up by intraperitoneal macrophages within a short period (between thirty minutes and one hour), and 60% of the composition is accumulated in breast tissue within a few hours to twelve hours. This faster delivery and high efficiency is an unexpected result, which is achieved by the drug delivery composition as claimed. Applicant submits that such unexpected results are not suggested by the cited art and could not have been predicted by the art.

Applicant's arguments are acknowledged, however they are not found persuasive because they are directed to limitations which are not in the claims. And even if the claim would recite accumulation in breast tissue, it is noted that all that is required for the rapid accumulation is intraperitoneal inoculation, which is already taught by Shimizu et al. Therefore, the liposomes of Shimizu et al. must necessarily accumulate in the breast tissue within a few hours to twelve hours.

14. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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